

PATENT ABSTRACTS OF JAPAN

(11)Publication number : 10-000190

(43)Date of publication of application : 06.01.1998

(51)Int.Cl.

A61B 5/14
G01N 21/35
G01N 33/483

(21)Application number : 08-154398

(71)Applicant : MATSUSHITA ELECTRIC WORKS
LTD

(22)Date of filing : 14.06.1996

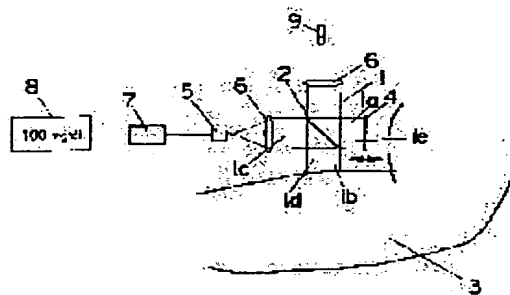
(72)Inventor : MARUO KATSUHIKO

(54) MEASURING DEVICE FOR PROPERTIES OF ORGANISM TISSUE

(57)Abstract:

PROBLEM TO BE SOLVED: To provide a measuring device which can make accurate quantitative or qualitative analysis of the properties of organism tissue by making more district the signals related to the concentration change and physical property change of the component and the tissue.

SOLUTION: A measuring device for the properties of a organism tissue, which measures organism tissue properties in a organism 3 non-invasively, is composed of a beam splitter 2 to divide into two beams the near infrared rays 1 which are coherent or similar to it, a reflection mirror 4 to reflect one of the split beams 1a of the infrared rays so that it 1a interferes with the other beams 1b which has been reflected by the vital organism structure, a sensor 5 to sense the signal according to the reflective beam 1c having undergone an interference, and an information processing means 7 to make computational processing of the signal sensed by the sensor 5. It is arranged so that the position of the reflection mirror 4 relative to the reflective beam 1d reflected by the organism tissue can be set any as desired.



LEGAL STATUS

[Date of request for examination]

[Date of sending the examiner's decision of rejection]

[Kind of final disposal of application other than the examiner's decision of rejection or application converted registration]

[Date of final disposal for application]

[Patent number]

[Date of registration]

[Number of appeal against examiner's decision of rejection]

[Date of requesting appeal against examiner's decision of rejection]

BEST AVAILABLE COPY

[Date of extinction of right]

Copyright (C); 1998,2003 Japan Patent Office

THIS PAGE BLANK (USPTO)

JAPANESE [JP,10-000190,A]

CLAIMS DETAILED DESCRIPTION TECHNICAL FIELD PRIOR ART EFFECT OF THE
INVENTION TECHNICAL PROBLEM MEANS DESCRIPTION OF DRAWINGS DRAWINGS

[Translation done.]

* NOTICES *

JPO and NCIPi are not responsible for any damages caused by the use of this translation.

- 1.This document has been translated by computer. So the translation may not reflect the original precisely.
- 2.*** shows the word which can not be translated.
- 3.In the drawings, any words are not translated.

CLAIMS

[Claim(s)]

[Claim 1] the body tissue in a living body -- the body tissue which measures description non-invasive -- description -- with the beam splitter which is a measuring device and divides a coherent or near-infrared light near it into two The reflecting mirror reflected so that one light may be made to interfere among the divided near-infrared light with the light of another side reflected by the body tissue, the body tissue characterized by forming the location of the reflecting mirror to the reflected light which was equipped with the detector which detects the signal of the reflected light made to interfere, and the information processing means which carries out data processing of the signal detected with the detector, and was reflected by the body tissue, enabling a free setup, and changing -- description -- a measuring device.

[Claim 2] said body tissue -- the body tissue according to claim 1 characterized by description being the body fluid constituent concentration in the cell of a body tissue, or besides the cell of a body tissue -- description -- a measuring device.

[Claim 3] said body tissue -- the body tissue according to claim 1 or 2 characterized by using the coherent near-infrared light of at least one kind of wavelength which consists of a part of all fields that the body fluid constituent concentration which is description is glucose concentration, and were chosen from the field (at least 950-1150nm and 1250-1800nm) in the quantum of said glucose concentration, or fields -- description -- a measuring device.

[Claim 4] the body tissue according to claim 1 to 3 characterized by setting up the location of said reflecting mirror and changing so that the reflected light reflected in the reflected light reflected by the body tissue between 0.1-10.0mm hypodermically with the reflecting mirror may be made to interfere -- description -- a measuring device.

[Claim 5] the body tissue according to claim 1 to 4 which said body tissue is the body surface close-attendants side of arterial blood tubing near the body surface, or venous blood tubing, and is characterized by setting up the location of said reflecting mirror and changing so that the reflected light reflected in the reflected light reflected by this body tissue with the reflecting mirror may be made to interfere -- description -- a measuring device.

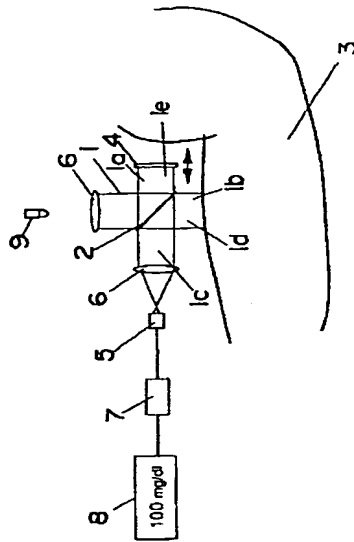
[Claim 6] the organization of a desired body tissue -- the body tissue according to claim 1 to 5 characterized by setting the location of said reflecting mirror as measuring description, and growing into it based on measurement of the size of the absorption of light of the petrographic constituent which is not desirable -- description -- a measuring device.

[Claim 7] the body tissue according to claim 6 characterized by detecting the size of the above-mentioned coherent near-infrared absorption of light in fat tissue by moving a reflecting mirror while using the coherent near-infrared light which said petrographic constituent which is not desirable is fat tissue, and becomes from a part of all field of one [at least] wavelength field (900-950nm and 1350-1420nm), or field -- description -- a measuring device.

[Claim 8] said body tissue -- the body tissue according to claim 1 characterized by descriptions being physical properties, such as hardness of a body tissue, and a consistency, -- description -- a measuring device.

[Translation done.]

Drawing selection Representative drawing



- 1 近赤外線
- 1a 光
- 1b 光
- 1c 干渉された反射光
- 1d 反射光
- 1e 反射光
- 2 ビームスプリッタ
- 3 生体
- 4 反射鏡
- 5 発出器
- 7 情報処理手段

[Translation done.]

* NOTICES *

JPO and NCIP1 are not responsible for any damages caused by the use of this translation.

- 1.This document has been translated by computer. So the translation may not reflect the original precisely.
- 2.**** shows the word which can not be translated.
- 3.In the drawings, any words are not translated.

DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[Field of the Invention] the body tissue to which this invention measures concentration, such as a glucose in blood, cholesterol, neutral fat, and a protein component, non-invasive especially using a near-infrared method about the measuring machine machine which measures the concentration of the indicator ingradient in body fluid, such as blood and cell sap, by non-invasion for the therapy of the health care or the illness -- description -- the body tissue which measures change of the body tissue represented by a measuring device or stiffness in shoulder and a breast cancer, liver cirrhosis, a fatty liver, and arteriosclerosis -- description -- it is related with a measuring device.

[0002]

[Description of the Prior Art] The measuring method of the glucose concentration in blood (blood sugar level) is explained about measurement of the conventional body fluid constituent concentration. The blood sugar meter used widely now is called the so-called biosensor which is made to carry out the chemical reaction of the glucose in the blood which collected blood, and measures glucose concentration. The fundamental biosensor consists of a part which identifies a measuring object component alternatively, and a part which changes into an electrical signal change which produces this measuring object component in the matter discernment by the part identified alternatively. The device with various electrochemistry measurement device, thermistor, field effect transistor (FET), photo transistor, etc. is used for the part changed into said electrical signal.

[0003] Moreover, the biological substances used for a matter discernment part (part which identifies said measuring object component alternatively) are cells (cell), such as an enzyme (enzyme), an antibody (antibody), binding protein (binding protein), lectin (lectin), an intracellular organelle (organelle), and a microorganism, an organization (tissue), etc., and these biological substances have the function to identify the specific matter. A biosensor is classified into an enzyme sensor, a microbial sensor, an immune sensor, an organelle sensor, and an organization sensor according to the biological substance to be used.

[0004] the enzyme which will be used for glucose detection if the glucose sensor by the enzyme electrode (matter discernment part using the enzyme as a biological substance) is taken for an example as an example of a blood sugar meter -- glucose oxidase (GOD) it is . This enzyme (GOD) The thing of the format which carries out the quantum of the glucose concentration because oxygen is consumed and the glucose sensor fixed in the poly membrane etc. catches change of this oxygen when the glucose in measurement liquid contacts the GOD fixed film is developed. A such blood collecting-type blood sugar meter is marketed widely, and is used for management of a diabetic's blood sugar level.

[0005] Moreover, the detection approach of a glucose as shown in JP,60-236631,A or JP,5-58735,B is one of things of the non-invasion which does not need blood collecting. The near-infrared light irradiated by the living body part is divided into a reference signal and a measurement signal, and the technique of measuring the blood sugar level is indicated by carrying out data processing of these values by these official reports. a source of the white light like [as the light source of near-infrared light] a tungsten halogen lamp in the above-mentioned technique -- a spectrum like an interference filter -- the approach and semi-conductor light emitting device (LED) which carry out a spectrum to wavelength predetermined

with a means are used. Moreover, as a detector of the near-infrared light which penetrated the living body part, the photodiode or a photo detector like a photo transistor is used. However, at present, these techniques have not reached practical use level.

[0006] The spectral analysis of the body fluid component by the above near-infrared light is the technique of attracting attention in recent years, and by the spectral analysis in a near infrared region as compared with the spectral analysis in an inside infrared region Since the water absorption spectrum is small, analysis of a water-solution system is possible, While it has the advantage in which the capacity which penetrates a living body is high, the signal level which belongs to molecular vibration has about 1/100, a small thing, and the demerit in which it is hard to specify attribution of a signal, as compared with an inside red field.

[0007] That is, when detecting the signal (signal) of the component (body fluid component) made into the purpose in a near infrared region, it has that the signal corresponding to concentration change of a component (body fluid component) made into the purpose is very small, and the problem that attribution of the signal is not clear in many cases. In order to solve such a problem, the so-called chemometrics technique combined with the statistical analysis technique or the multivariate-analysis technique (MLR), for example, a linearity multiple regression analysis, principal component regression analysis, and PLS regression analysis (partial least squares regressin) is used. However, although it is the technique excellent in such statistical analysis technique catching a minute signal change, and performing exact measuring (calibration), magnitude (SN ratio) of the signal (signal) of the target component (body fluid component) is not improved.

[0008] Then, a difference with the signal related to [for an improvement of an SN ratio / in / at the former / a near infrared region] concentration change of the component (body fluid component) of a reference signal and the purpose, Or the technique of having ****ed the noise component small enough and carrying out it is used by taking those ratios by clarifying concentration change (fluctuation) of the target component (body fluid component), or equalizing the signal (signal related to concentration change of the target component (body fluid component)) which carried out multiple-times measurement. Especially the above-mentioned equalization technique is used for various measurement from removal of a noise component being simply possible by making [many] the count of an average (count of measurement of a signal).

[0009] Moreover, by the conventional approach of making only carry out incidence of the light to a body tissue, and measuring the transmitted light or reflected light, it will be measured as a signal in the form which the transmitted lights or the reflected lights from an organization other than a body tissue to consider quantification of description as an intention superimposed, and has become the cause by which a noise component becomes large. then, description -- in measurement, the establishment and equipment of technique which can perform spectrum measurement (spectral-analysis measurement) of the form where the target organization is aimed at and moved are desired so that only the transmitted light or the reflected light from a body tissue to consider quantification of description as an intention may be obtained.

[0010]

[Problem(s) to be Solved by the Invention] therefore, the body tissue of non-invasion without the need of carrying out invasion of blood or the cell sap, and taking it out with a hypodermic needle etc. in case this invention measures the concentration of a living body's body fluid component -- description -- a measuring device -- It is a thing aiming at offering a measuring device. or physical properties, such as hardness of an organization in the living body, and a consistency, -- non-invasion and the body tissue measured in non-contact -- description -- in detail a near-infrared spectral-analysis method -- a body tissue -- description -- the reflected light of a from the organization aiming at analysis, or near the organization by detecting alternatively, when it is adapted for measurement and performs the quantum or qualitative analysis of a component of the purpose under organization the signal relevant to concentration change and physical-properties change of a component and an organization -- more -- clear -- carrying out -- an exact body tissue -- the body tissue which can perform the quantitative analysis or qualitative analysis of description -- description -- it aims at offering a measuring device.

[0011]

[Means for Solving the Problem] the body tissue of this invention according to claim 1 --

description -- a measuring device the body tissue in a living body 3 -- the body tissue which measures description non-invasive -- description -- with the beam splitter 2 which is a measuring device and divides the coherent or near-infrared light 1 near it into two The reflecting mirror 4 reflected so that one optical 1a may be made to interfere among the divided near-infrared light with optical 1b of another side reflected by the body tissue, It has the detector 5 which detects the signal of reflected light 1c made to interfere, and the information processing means 7 which carries out data processing of the signal detected with the detector 5, and is characterized by forming the location of the reflecting mirror 4 to 1d of reflected lights reflected by the body tissue, enabling a free setup, and changing.

[0012] moreover, the body tissue of this invention according to claim 2 -- description -- a measuring device -- the configuration of claim 1 -- in addition, said body tissue -- it is characterized by description being the body fluid constituent concentration in the cell of a body tissue, or besides the cell of a body tissue. moreover, the body tissue of this invention according to claim 3 -- description -- a measuring device -- claim 1 or the configuration of 2 -- in addition, said body tissue -- the body fluid constituent concentration which is description is glucose concentration, and it is characterized by using the coherent near-infrared light of at least one kind of wavelength which consists of a part of all fields chosen from the field (at least 950-1150nm and 1250-1800nm) in the quantum of said glucose concentration, or fields.

[0013] moreover, the body tissue of this invention according to claim 4 -- description -- a measuring device -- the configuration of claim 1 thru/or either of 3 -- in addition, it is characterized by setting up the location of said reflecting mirror 4 and changing so that reflected light 1e reflected in 1d of reflected lights reflected by the body tissue between 0.1-10.0mm hypodermically with the reflecting mirror 4 may be made to interfere. moreover, the body tissue of this invention according to claim 5 -- description -- a measuring device -- the configuration of claim 1 thru/or either of 4 -- in addition, said body tissue is the body surface close-attendants side of arterial blood tubing near the body surface, or venous blood tubing, and it is characterized by setting up the location of said reflecting mirror 4 and changing so that reflected light 1e reflected in 1d of reflected lights reflected by this body tissue with said reflecting mirror 4 may be made to interfere.

[0014] moreover, the body tissue of this invention according to claim 6 -- description -- a measuring device -- the configuration of claim 1 thru/or either of 5 -- in addition, the organization of a desired body tissue -- it is characterized by setting the location of a reflecting mirror 4 as measuring description, and growing into it based on measurement of the size of the absorption of light of the petrographic constituent which is not desirable. moreover, the body tissue of this invention according to claim 7 -- description -- a measuring device In addition to a configuration according to claim 6, said petrographic constituent which is not desirable is fat tissue. While using the coherent near-infrared light 1 which consists of a part of all field of one [at least] wavelength field (900-950nm and 1350-1420nm), or field It is characterized by detecting the size of absorption of said coherent near-infrared light 1 in fat tissue by moving a reflecting mirror 4.

[0015] moreover, the body tissue of this invention according to claim 8 -- description -- a measuring device -- the configuration of claim 1 -- in addition, said body tissue -- it is characterized by descriptions being physical properties, such as hardness of a body tissue, and a consistency.

[0016]

[Embodiment of the Invention] Hereafter, the gestalt of operation of this invention is explained. the body tissue shown in drawing 1 -- description -- if the coherent or near-infrared light 1 near it can be obtained on the wavelength of 750-2500nm as the light source 9 used in a measuring device, either can be used, for example, what processed the light of the laser light source, the thing which processed the light of a halogen lamp using the diffraction grating, the interferometer, the filter, etc., the LED light source, or the LED light source using the diffraction grating, the interferometer, the filter, etc. can be used.

[0017] As a beam splitter 2, if the above-mentioned near-infrared light 1, such as a half mirror, can be divided into two, either can be used and this beam splitter 2 is arranged between the above-mentioned light source 9 and a living body 3. As a reflecting mirror 4, one optical 1a of the light divided into two by the above-mentioned beam splitter 2 is reflected, and it is arranged in the location which optical 1a of one of these is drawn, and reaches. Moreover, the reflecting

mirror 4 is formed free [migration] so that the location to 1d of reflected lights reflected by the body tissue in the living body 3 which mentions later may be changed and it can set up freely.

[0018] As a detector 5, be [what is necessary / just although it has a light-receiving property in a near infrared region (near-infrared light 1)], in the near infrared region whose wavelength is 600-1100nm, the detector made from InGaAs can use suitably especially in the near infrared region whose wavelength the detector made from Si is 700-1700nm. If the signal from reflected light 1c which is obtained with a detector 5, which is mentioned later and in which it interfered is inputted as a data-processing means 7 and data processing of this signal can be carried out, either can be used and microcomputer PYUTA etc. can be illustrated.

[0019] With the above-mentioned data-processing means 7, the shape of raw somatic, for example, glucose concentration etc., is computed by carrying out data processing of the signal from reflected light 1c which is obtained with a detector 5 and in which it interfered according to the calibration curve prepared beforehand. The statistical analysis technique or the multivariate-analysis technique (MLR), for example, a linearity multiple regression analysis, principal component regression analysis, PLS regression analysis (partial least squares regressin), and the neural network technique can be used for creation of a calibration curve (measuring type). Such statistical analysis technique is the technique excellent in catching a minute signal change and performing exact measuring (calibration).

[0020] next, top Norio body tissue -- description -- actuation of a measuring device is explained. The near-infrared light 1 first irradiated from the light source 9 is divided into optical 1a drawn in the direction of a reflecting mirror 4, and optical 1b drawn in the direction of a living body 3 by the beam splitter 2. Next, while being reflected with a reflecting mirror 4 and setting to reflected light 1e optical 1a drawn in the direction of a reflecting plate 4, it is reflected by the body tissue inside a living body 3, and optical 1b drawn in the direction of a living body 3 becomes 1d of reflected lights which are the scattered light. Next, 1d of reflected lights reflected by the body tissue and reflected light 1e reflected with the reflecting mirror 4 interfere, and this reflected light 1c in which it interfered is led to a detector 5. And by carrying out data processing of the signal acquired from reflected light 1c which was led to the detector 5 next, and in which it interfered as mentioned above with the information processing means 7, the quantum of the description of the body tissue of a request aiming at measurement can be carried out, and it can be measured.

[0021] Since the spectral-analysis approach using near-infrared light (near infrared region) with a wavelength of 750-2500nm currently performed from the former as mentioned above has a small signal (signal) relevant to the component generally made into the purpose and the attribution is not clear in many cases, quantitative analysis is carried out difficult. For this reason, at the former, in order to improve an SN ratio, the difference of a certain criteria signal and purpose signal (signal from the body tissue aiming at measurement) is taken, or it pretreats taking and standardizing that ratio etc., and the quantum of the component of the purpose of the target body tissue is performed by applying the multivariate-analysis technique.

[0022] moreover, the light from a certain light source which contains two or more wavelength by the conventional spectral-analysis approach -- an interference filter or a diffraction grating -- serial -- a spectrum -- carrying out -- the light by which the spectrum was carried out -- one by one -- a ratio -- a measurement object is irradiated and it is asking for the absorbance and transmittance in each wavelength range by detecting the intensity of light penetrated or reflected, respectively. however, this technique -- a body tissue -- when it applies to measurement of description, it is detected as a spectrum which all the information that belongs to the constituent of the complicated body tissue which light penetrates or reflects superimposed -- ***** -- getting it blocked -- it becomes the spectrum with which the signal which originates in addition to the body tissue of the request which considers measurement as an intention (purpose) (attribution) was also contained. Therefore, the noise component to the signal which belongs to the component of the body tissue of the target request will increase, and an SN ratio will fall.

[0023] however, this invention top Norio body tissue -- description -- in a measuring device Since 1d of reflected lights reflected by the body tissue and reflected light 1e reflected with the reflecting mirror 4 are made to interfere and it was made to lead to a detector 5 The reflected light reflected light 1e reflected with the reflecting mirror 4 among 1d of reflected lights

reflected by the body tissue and whose phase correspond can be strengthened, and it can lead to a detector 5. The noise component to the signal which belongs to the component of a body tissue which reflects the reflected light reflected light 1e reflected with the reflecting mirror 4 and whose phase correspond can be reduced, and an SN ratio can be raised.

[0024] The distance between the body tissue which reflects the reflected light reflected light 1e reflected with the reflecting mirror 4 and whose phase correspond, and reflected light 1e and the point in which 1d interferes mutually It is the distance and the match between a reflecting mirror 4, and said reflected light 1e and the point in which 1d interferes mutually. Therefore, it is detectable whether the reflected light reflected from the body tissue of the location of living body 3 throat is strengthened by interference by finding the distance between the points in which a reflecting mirror 4, said reflected light 1e, and 1d of reflected lights interfere.

[0025] Moreover, since the above-mentioned reflecting mirror 4 was formed free [migration] to 1d of reflected lights reflected by the body tissue, the location of the point in which reflected light 1e and 1d of reflected lights interfere, and a reflecting mirror 4 can be set up freely.

Therefore, by moving a reflecting mirror 4 to the point in which above-mentioned reflected light 1e and 1d of reflected lights interfere The phase of the reflected light from the body tissue which exists in the location of the arbitration in a living body's 3 depth direction, and the phase of reflected light 1e reflected with a reflecting mirror 4 can be made in agreement. The reflected light from the body tissue of the request set as the object of measurement can be strengthened alternatively, the noise component to the signal which belongs to the component of a desired body tissue set as the object of measurement can be reduced, and an SN ratio can be raised.

[0026] the body tissue of this invention -- description -- a measuring device sets the quantum of the concentration of the body fluid component in a body tissue cell or besides a body tissue cell as one purpose. on the other hand, it is in the quantum of the concentration of this body fluid component among the near-infrared light 1 of the field (1250-1800nm) near the first overtone of water, and the near-infrared light 1 of the field (800-1300nm) near the second harmonic overtone of water -- it is -- it carries out by using both. As a property of each field, in the field near the first overtone of water, while the spectrum signal which belongs to molecular vibration is large, the permeability of light is bad, and while the spectrum signal which belongs to molecular vibration in the field near the second harmonic overtone of water is small, it is rich in the permeability of light.

[0027] moreover, when the quantum of the concentration of the above-mentioned body fluid component is a quantum of glucose concentration The coherent near-infrared light of at least one kind of wavelength which consists of a part of all fields chosen from the wavelength field (950-1150nm and 1250-1800nm), or fields as a near-infrared light 1 irradiated from the light source 9, Especially, it is necessary to use wavelength (945**20nm, 965**20nm, 1015**30nm, 1100**30nm, 1400**20nm, 1450**20nm, 1500**20nm, and 1680**20nm) of coherent near-infrared light.

[0028] In the quantum of glucose concentration, as a signal of the field near the first overtone of water, that is, 950-1150nm, Preferably 945**20nm, 965**20nm, 1015**30nm, It is necessary to measure preferably 1250-1800nm 1100**30nm, using at least one wave of a signal (1400**20nm, 1450**20nm, 1500**20nm, and 1680**20nm) as a signal of the field near the second harmonic overtone of water.

[0029] Thus, precision can carry out preferably 950-1150nm of 1250-1800nm of glucose concentration quantitative analysis to the quantum of glucose concentration by using at least one wave of a signal (1400**20nm, 1450**20nm, 1500**20nm, and 1680**20nm) (near-infrared light 1) for 945**20nm, 965**20nm, 1015**30nm, and 1100**30nm preferably, and measuring.

[0030] The signal of each measured wavelength is changed into glucose concentration with the information processing means 7 using the calibration curve (measuring type) created beforehand, and is displayed as measured value with a display 8. Although creation of a calibration curve (measuring type) is usually created using some kinds of wavelength, if said wavelength is included in this invention, neither measurement wavelength nor a number will be restricted.

[0031] Moreover, in order to carry out the quantum of the glucose concentration in a body tissue cell or besides a body tissue cell as a substitution property of the blood sugar level The location of a reflecting mirror 4 can be set up so that it may be made to interfere in 1d (scattered light) of reflected lights from the body tissue made the purpose which is in the

location between 0.5-10.0mm preferably between 0.1-10.0mm hypodermically (object of measurement), and it is this. Precision can carry out glucose concentration as a substitution property of the blood sugar level quantitative analysis.

[0032] moreover, in performing a quantum for the quantum of concentration, especially glucose concentration of the body fluid component in a body tissue cell or besides a body tissue cell, reflected light 1e from a reflecting mirror 4 is made to interfere in 1d of reflected lights from the artery which flows near a living body's 3 body surface, or a vein, and it measures -- it is a very good approach. If the location of a reflecting mirror 4 is adjusted and set up in that case so that the reflected light in the body tissue of the side near [where optical 1b of another side divided by the beam splitter 2 of the near-infrared light 1 is irradiated] the near blood vessel (i.e., the body surface close attendants of a blood vessel) may interfere with reflected light 1e from a reflecting mirror 4, since the flowing blood has the property that dispersion is large and cannot use a blood vessel for measurement easily, a good spectrum (signal) will be obtained.

[0033] Moreover, it is necessary to measure by avoiding a subcutaneous adipose tissue in the quantum of glucose concentration from a viewpoint of obtaining a spectrum with a sufficient (high) SN ratio. Therefore, if it is very effective to move the location of a reflecting mirror 4 and to find the suitable setting location in measurement and it is in charge of detecting the location of the fat tissue, it carries out to the quantum of glucose concentration using the characteristic absorption of light of the fat tissue which is not desirable. In measuring size of the absorption of light in this fat tissue, it carries out using the coherent near-infrared light 1 which consists of a part of all field of a wavelength field (at least 900-950nm or 1350-1420nm), or field, and it compares whether it is that which this absorption calls at fat tissue, and judges.

[0034] the body tissue of this invention -- description -- another purpose of a measuring device -- a body tissue -- description is physical properties like the hardness of a body tissue, or a consistency, and is about these physical properties to carry out [qualitative analysis or] quantitative analysis. Physical properties like the hardness of a body tissue or a consistency are stiffness of the body specifically represented by stiffness in shoulder or change of the body tissue represented by a breast cancer, liver cirrhosis, a fatty liver, and arteriosclerosis.

[0035] such a body tissue -- the spectrum obtained from many test subjects is carried out to analysis of description using quantitative analysis or qualitative analysis. A linearity multiple regression analysis (MLR), principal component regression analysis, PLS regression analysis (partial least squares regressin), the neural network technique, and the neural network technique are used for quantitative analysis, and technique, such as discriminant analysis and a cluster analysis, can be used for qualitative analysis.

[0036] the body tissue which analyzes physical properties like the hardness of a body tissue, or a consistency (measurement) -- description -- a measuring device as well as the above can be formed. Although the decision of the measuring technique in the wavelength and the information-processing means 7 of the near-infrared light 1 irradiated from the light source 9 used for analysis performs by analyzing the spectrum (a signal) of much normal tissues and a lesion organization, as other decision technique of the measuring technique in the wavelength and the information-processing means 7 of the near-infrared light 1 irradiated from the light source 9 used for analysis, there is the approach of performing in invasion by an animal experiment etc. beforehand. This approach by irradiating the light which carried out the spectrum to the measured organization (both normal tissue and a lesion organization) which made it expose in invasion by technique, such as a diffraction grating and FT-IR, obtaining an absorption spectrum, and carrying out multivariate analysis of this absorption spectrum The measuring technique in the wavelength and the information processing means 7 of the near-infrared light 1 of using for a measuring device is determined. the body tissue of this invention -- description -- the measuring technique in this wavelength and information processing means 7 of the near-infrared light 1 that were determined -- using -- above -- the body tissue of this invention -- description -- the body tissue by the measuring device -- measurement of description (inch vivo measurement) It is made to carry out.

[0037] If an example is given, the cancer organization of a mouse which made it cancerate artificially will be exposed by cutting epidermal tissue open, and the spectrum of a cancer organization will be obtained by the above-mentioned technique. moreover, the thing which same actuation is carried out to the mouse of a large number containing a normal mouse, and a spectrum is obtained, and then is done for the qualitative analysis of these spectrums -- an

organization -- the wavelength distinction of description has a meaning -- taking up -- the body tissue of this invention -- description -- the wavelength of the near-infrared light 1 used for a measuring device is determined. and the near-infrared light 1 of this determined wavelength -- the body tissue of this invention -- description -- by analyzing description of the body tissue by the measuring device, the cancer onset can be distinguished by the body tissue. [0038] in addition, the body tissue of this invention -- description -- for raising the analysis precision of a measuring device -- further -- the body tissue of this invention -- description -- it is necessary to perform and carry out multivariate analysis of the analysis by the measuring device to many body tissues non-invasive

* NOTICES *

JPO and NCIP I are not responsible for any damages caused by the use of this translation.

- 1.This document has been translated by computer. So the translation may not reflect the original precisely.
- 2.**** shows the word which can not be translated.
- 3.In the drawings, any words are not translated.

TECHNICAL FIELD

[Field of the Invention] the body tissue to which this invention measures concentration, such as a glucose in blood, cholesterol, neutral fat, and a protein component, non-invasive especially using a near-infrared method about the measuring machine machine which measures the concentration of the indicator ingradient in body fluid, such as blood and cell sap, by non-invasion for the therapy of the health care or the illness -- description -- the body tissue which measures change of the body tissue represented by a measuring device or stiffness in shoulder and a breast cancer, liver cirrhosis, a fatty liver, and arteriosclerosis -- description -- it is related with a measuring device.

[Translation done.]

* NOTICES *

JPO and NCIP1 are not responsible for any damages caused by the use of this translation.

1.This document has been translated by computer. So the translation may not reflect the original precisely.

2.*** shows the word which can not be translated.

3.In the drawings, any words are not translated.

PRIOR ART

[Description of the Prior Art] The measuring method of the glucose concentration in blood (blood sugar level) is explained about measurement of the conventional body fluid constituent concentration. The blood sugar meter used widely now is called the so-called biosensor which is made to carry out the chemical reaction of the glucose in the blood which collected blood, and measures glucose concentration. The fundamental biosensor consists of a part which identifies a measuring object component alternatively, and a part which changes into an electrical signal change which produces this measuring object component in the matter discernment by the part identified alternatively. The device with various electrochemistry measurement device, thermistor, field effect transistor (FET), photo transistor, etc. is used for the part changed into said electrical signal.

[0003] Moreover, the biological substances used for a matter discernment part (part which identifies said measuring object component alternatively) are cells (cell), such as an enzyme (enzyme), an antibody (antibody), binding protein (binding protein), lectin (lectin), an intracellular organelle (organelle), and a microorganism, an organization (tissue), etc., and these biological substances have the function to identify the specific matter. A biosensor is classified into an enzyme sensor, a microbial sensor, an immune sensor, an organelle sensor, and an organization sensor according to the biological substance to be used.

[0004] the enzyme which will be used for glucose detection if the glucose sensor by the enzyme electrode (matter discernment part using the enzyme as a biological substance) is taken for an example as an example of a blood sugar meter -- glucose oxidase (GOD) it is . This enzyme (GOD) The thing of the format which carries out the quantum of the glucose concentration because oxygen is consumed and the glucose sensor fixed in the poly membrane etc. catches change of this oxygen when the glucose in measurement liquid contacts the GOD fixed film is developed. A such blood collecting-type blood sugar meter is marketed widely, and is used for management of a diabetic's blood sugar level.

[0005] Moreover, the detection approach of a glucose as shown in JP,60-236631,A or JP,5-58735,B is one of things of the non-invasion which does not need blood collecting. The near-infrared light irradiated by the living body part is divided into a reference signal and a measurement signal, and the technique of measuring the blood sugar level is indicated by carrying out data processing of these values by these official reports. a source of the white light like [as the light source of near-infrared light] a tungsten halogen lamp in the above-mentioned technique -- a spectrum like an interference filter -- the approach and semi-conductor light emitting device (LED) which carry out a spectrum to wavelength predetermined with a means are used. Moreover, as a detector of the near-infrared light which penetrated the living body part, the photodiode or a photo detector like a photo transistor is used. However, at present, these techniques have not reached practical use level.

[0006] The spectral analysis of the body fluid component by the above near-infrared light is the technique of attracting attention in recent years, and by the spectral analysis in a near infrared region as compared with the spectral analysis in an inside infrared region Since the water absorption spectrum is small, analysis of a water-solution system is possible, While it has the advantage in which the capacity which penetrates a living body is high, the signal level which belongs to molecular vibration has about 1/100, a small thing, and the demerit in which it is hard to specify attribution of a signal, as compared with an inside red field.

[0007] That is, when detecting the signal (signal) of the component (body fluid component)

made into the purpose in a near infrared region, it has that the signal corresponding to concentration change of a component (body fluid component) made into the purpose is very small, and the problem that attribution of the signal is not clear in many cases. In order to solve such a problem, the so-called chemometrics technique combined with the statistical analysis technique or the multivariate-analysis technique (MLR), for example, a linearity multiple regression analysis, principal component regression analysis, and PLS regression analysis (partial least squares regressin) is used. However, although it is the technique excellent in such statistical analysis technique catching a minute signal change, and performing exact measuring (calibration), magnitude (SN ratio) of the signal (signal) of the target component (body fluid component) is not improved.

[0008] Then, a difference with the signal related to [for an improvement of an SN ratio / in / at the former / a near infrared region] concentration change of the component (body fluid component) of a reference signal and the purpose, Or the technique of having ****ed the noise component small enough and carrying out it is used by taking those ratios by clarifying concentration change (fluctuation) of the target component (body fluid component), or equalizing the signal (signal related to concentration change of the target component (body fluid component)) which carried out multiple-times measurement. Especially the above-mentioned equalization technique is used for various measurement from removal of a noise component being simply possible by making [many] the count of an average (count of measurement of a signal).

[0009] Moreover, by the conventional approach of making only carry out incidence of the light to a body tissue, and measuring the transmitted light or reflected light, it will be measured as a signal in the form which the transmitted lights or the reflected lights from an organization other than a body tissue to consider quantification of description as an intention superimposed, and has become the cause by which a noise component becomes large. then, description — in measurement, the establishment and equipment of technique which can perform spectrum measurement (spectral-analysis measurement) of the form where the target organization is aimed at and moved are desired so that only the transmitted light or the reflected light from a body tissue to consider quantification of description as an intention may be obtained.

[Translation done.]

* NOTICES *

JPO and NCIP are not responsible for any damages caused by the use of this translation.

- 1.This document has been translated by computer. So the translation may not reflect the original precisely.
- 2.*** shows the word which can not be translated.
- 3.In the drawings, any words are not translated.

EFFECT OF THE INVENTION

[Effect of the Invention] As mentioned above invention of this invention according to claim 1 The beam splitter which divides a coherent or near-infrared light near it into two, The reflecting mirror reflected so that one light may be made to interfere among the divided near-infrared light with the light of another side reflected by the body tissue, Since the location of the reflecting mirror to the reflected light which was equipped with the detector which detects the signal of the reflected light made to interfere, and the information processing means which carries out data processing of the signal detected with the detector, and was reflected by the body tissue was formed enabling a free setup By reflecting with a reflecting mirror so that one light may be made to interfere among the divided near-infrared light with the light of another side reflected by the body tissue The reflected light reflected by the body tissue of the phase of the reflected light reflected with the reflecting mirror and a phase in agreement can be strengthened alternatively. the description of the body tissue which reflects the reflected light of the phase of the reflected light reflected with the reflecting mirror, and a phase in agreement -- analysis can be analyzed with a sufficient precision by non-invasion -- that is, the signal relevant to concentration change and physical-properties change of the component of a body tissue and an organization -- more -- clear -- carrying out -- an exact body tissue -- the quantitative analysis or qualitative analysis of description can be performed.

[0059] And by forming the location of the reflecting mirror to the reflected light reflected by the body tissue, enabling a free setup, the phase of the reflected light from the body tissue of the location a living body's arbitration and the phase of the reflected light reflected with the reflecting mirror can be made in agreement, and the reflected light of a from near [of a location] a living body's arbitration the organization aiming at analysis or near the organization can be detected alternatively.

[0060] moreover, invention of this invention according to claim 2 -- said body tissue -- since description is the body fluid constituent concentration in the cell of a body tissue, or besides the cell of a body tissue, the body fluid constituent concentration in the cell of a body tissue or besides the cell of a body tissue can be analyzed with a sufficient precision by non-invasion. moreover, invention of this invention according to claim 3 -- said body tissue -- since the coherent near-infrared light of at least one kind of wavelength which consists of a part of all fields that the body fluid constituent concentration which is description is glucose concentration, and were chosen from the field (at least 950-1150nm and 1250-1800nm) in the quantum of said glucose concentration, or fields was used, glucose concentration can be analyzed with a sufficient precision by non-invasion.

[0061] Moreover, in measuring the glucose concentration of a body tissue as a substitution property of the blood sugar level, since the location of said reflecting mirror was set up so that the reflected light reflected in the reflected light reflected by the body tissue between 0.1-10.0mm hypodermically with the reflecting mirror might be made to interfere, invention of this invention according to claim 4 can analyze glucose concentration with a sufficient precision by non-invasion.

[0062] Moreover, said body tissue of invention of this invention according to claim 5 is the body surface close-attendants side of arterial blood tubing near the body surface, or venous blood tubing. Since the location of said reflecting mirror was set up so that the reflected light reflected in the reflected light reflected by this body tissue with the reflecting mirror might be made to interfere By making in agreement the phase of the reflected light from the body

surface close-attendants side of arterial blood tubing near [small] the body surface of dispersion, or venous blood tubing, and the phase of the reflected light reflected with the reflecting mirror Rather than the case where the phase of the reflected light from the large blood of dispersion and the phase of the reflected light reflected with the reflecting mirror are made in agreement, the shape of raw somatic and glucose concentration can be analyzed with a sufficient precision by non-invasion.

[0063] moreover, invention of this invention according to claim 6 -- the organization of a desired body tissue, since the location of said reflecting mirror was set as measuring description based on measurement of the size of the absorption of light of the petrographic constituent which is not desirable the organization of a desired body tissue -- in agreement with measuring description in the phase of the reflected light from the petrographic constituent which is not desirable, and the phase of the reflected light reflected with the reflecting mirror -- not making -- making -- a living body -- description can be analyzed with a sufficient precision by non-invasion.

[0064] Moreover, since invention of this invention according to claim 7 detected the size of the above-mentioned coherent near-infrared absorption of light in fat tissue by moving a reflecting mirror while using the coherent near-infrared light which said petrographic constituent which is not desirable is fat tissue, and becomes from a part of all field of one [at least] wavelength field (900-950nm and 1350-1420nm), or field, it can analyze with a sufficient precision whether it is the reflected light from fat tissue.

[0065] moreover, invention of this invention according to claim 8 -- said body tissue -- since descriptions are physical properties, such as hardness of a body tissue, and a consistency, analysis of the above-mentioned physical properties can be analyzed with a sufficient precision by non-invasion among the descriptions of a body tissue.

[Translation done.]

* NOTICES *

JPO and NCIPi are not responsible for any damages caused by the use of this translation.

- 1.This document has been translated by computer. So the translation may not reflect the original precisely.
- 2.**** shows the word which can not be translated.
- 3.In the drawings, any words are not translated.

TECHNICAL PROBLEM

[Problem(s) to be Solved by the Invention] therefore, the body tissue of non-invasion without the need of carrying out invasion of blood or the cell sap, and taking it out with a hypodermic needle etc. in case this invention measures the concentration of a living body's body fluid component -- description -- a measuring device -- It is a thing aiming at offering a measuring device. or physical properties, such as hardness of an organization in the living body, and a consistency, -- non-invasion and the body tissue measured in non-contact -- description -- in detail a near-infrared spectral-analysis method -- a body tissue -- description -- the reflected light of a from the organization aiming at analysis, or near the organization by detecting alternatively, when it is adapted for measurement and performs the quantum or qualitative analysis of a component of the purpose under organization the signal relevant to concentration change and physical-properties change of a component and an organization -- more -- clear -- carrying out -- an exact body tissue -- the body tissue which can perform the quantitative analysis or qualitative analysis of description -- description -- it aims at offering a measuring device.

[Translation done.]

* NOTICES *

JPO and NCIPJ are not responsible for any damages caused by the use of this translation.

- 1.This document has been translated by computer. So the translation may not reflect the original precisely.
- 2.**** shows the word which can not be translated.
- 3.In the drawings, any words are not translated.

MEANS

[Means for Solving the Problem] the body tissue of this invention according to claim 1 -- description -- a measuring device the body tissue in a living body 3 -- the body tissue which measures description non-invasive -- description -- with the beam splitter 2 which is a measuring device and divides the coherent or near-infrared light 1 near it into two The reflecting mirror 4 reflected so that one optical 1a may be made to interfere among the divided near-infrared light with optical 1b of another side reflected by the body tissue, It has the detector 5 which detects the signal of reflected light 1c made to interfere, and the information processing means 7 which carries out data processing of the signal detected with the detector 5, and is characterized by forming the location of the reflecting mirror 4 to 1d of reflected lights reflected by the body tissue, enabling a free setup, and changing.

[0012] moreover, the body tissue of this invention according to claim 2 -- description -- a measuring device -- the configuration of claim 1 -- in addition, said body tissue -- it is characterized by description being the body fluid constituent concentration in the cell of a body tissue, or besides the cell of a body tissue. moreover, the body tissue of this invention according to claim 3 -- description -- a measuring device -- claim 1 or the configuration of 2 -- in addition, said body tissue -- the body fluid constituent concentration which is description is glucose concentration, and it is characterized by using the coherent near-infrared light of at least one kind of wavelength which consists of a part of all fields chosen from the field (at least 950-1150nm and 1250-1800nm) in the quantum of said glucose concentration, or fields.

[0013] moreover, the body tissue of this invention according to claim 4 -- description -- a measuring device -- the configuration of claim 1 thru/or either of 3 -- in addition, it is characterized by setting up the location of said reflecting mirror 4 and changing so that reflected light 1e reflected in 1d of reflected lights reflected by the body tissue between 0.1-10.0mm hypodermically with the reflecting mirror 4 may be made to interfere. moreover, the body tissue of this invention according to claim 5 -- description -- a measuring device -- the configuration of claim 1 thru/or either of 4 -- in addition, said body tissue is the body surface close-attendants side of arterial blood tubing near the body surface, or venous blood tubing, and it is characterized by setting up the location of said reflecting mirror 4 and changing so that reflected light 1e reflected in 1d of reflected lights reflected by this body tissue with said reflecting mirror 4 may be made to interfere.

[0014] moreover, the body tissue of this invention according to claim 6 -- description -- a measuring device -- the configuration of claim 1 thru/or either of 5 -- in addition, the organization of a desired body tissue -- it is characterized by setting the location of a reflecting mirror 4 as measuring description, and growing into it based on measurement of the size of the absorption of light of the petrographic constituent which is not desirable. moreover, the body tissue of this invention according to claim 7 -- description -- a measuring device In addition to a configuration according to claim 6, said petrographic constituent which is not desirable is fat tissue. While using the coherent near-infrared light 1 which consists of a part of all field of one [at least] wavelength field (900-950nm and 1350-1420nm), or field It is characterized by detecting the size of absorption of said coherent near-infrared light 1 in fat tissue by moving a reflecting mirror 4.

[0015] moreover, the body tissue of this invention according to claim 8 -- description -- a measuring device -- the configuration of claim 1 -- in addition, said body tissue -- it is characterized by descriptions being physical properties, such as hardness of a body tissue, and

a consistency.

[0016]

[Embodiment of the Invention] Hereafter, the gestalt of operation of this invention is explained. the body tissue shown in drawing 1 -- description -- if the coherent or near-infrared light 1 near it can be obtained on the wavelength of 750-2500nm as the light source 9 used in a measuring device, either can be used, for example, what processed the light of the laser light source, the thing which processed the light of a halogen lamp using the diffraction grating, the interferometer, the filter, etc., the LED light source, or the LED light source using the diffraction grating, the interferometer, the filter, etc. can be used.

[0017] As a beam splitter 2, if the above-mentioned near-infrared light 1, such as a half mirror, can be divided into two, either can be used and this beam splitter 2 is arranged between the above-mentioned light source 9 and a living body 3. As a reflecting mirror 4, one optical 1a of the light divided into two by the above-mentioned beam splitter 2 is reflected, and it is arranged in the location which optical 1a of one of these is drawn, and reaches. Moreover, the reflecting mirror 4 is formed free [migration] so that the location to 1d of reflected lights reflected by the body tissue in the living body 3 which mentions later may be changed and it can set up freely.

[0018] As a detector 5, be [what is necessary / just although it has a light-receiving property in a near infrared region (near-infrared light 1)], in the near infrared region whose wavelength is 600-1100nm, the detector made from InGaAs can use suitably especially in the near infrared region whose wavelength the detector made from Si is 700-1700nm. If the signal from reflected light 1c which is obtained with a detector 5, which is mentioned later and in which it interfered is inputted as a data-processing means 7 and data processing of this signal can be carried out, either can be used and microcomputer PYUTA etc. can be illustrated.

[0019] With the above-mentioned data-processing means 7, the shape of raw somatic, for example, glucose concentration etc., is computed by carrying out data processing of the signal from reflected light 1c which is obtained with a detector 5 and in which it interfered according to the calibration curve prepared beforehand. The statistical analysis technique or the multivariate-analysis technique (MLR), for example, a linearity multiple regression analysis, principal component regression analysis, PLS regression analysis (partial least squares regressin), and the neural network technique can be used for creation of a calibration curve (measuring type). Such statistical analysis technique is the technique excellent in catching a minute signal change and performing exact measuring (calibration).

[0020] next, top Norio body tissue -- description -- actuation of a measuring device is explained. The near-infrared light 1 first irradiated from the light source 9 is divided into optical 1a drawn in the direction of a reflecting mirror 4, and optical 1b drawn in the direction of a living body 3 by the beam splitter 2. Next, while being reflected with a reflecting mirror 4 and setting to reflected light 1e optical 1a drawn in the direction of a reflecting plate 4, it is reflected by the body tissue inside a living body 3, and optical 1b drawn in the direction of a living body 3 becomes 1d of reflected lights which are the scattered light. Next, 1d of reflected lights reflected by the body tissue and reflected light 1e reflected with the reflecting mirror 4 interfere, and this reflected light 1c in which it interfered is led to a detector 5. And by carrying out data processing of the signal acquired from reflected light 1c which was led to the detector 5 next, and in which it interfered as mentioned above with the information processing means 7, the quantum of the description of the body tissue of a request aiming at measurement can be carried out, and it can be measured.

[0021] Since the spectral-analysis approach using near-infrared light (near infrared region) with a wavelength of 750-2500nm currently performed from the former as mentioned above has a small signal (signal) relevant to the component generally made into the purpose and the attribution is not clear in many cases, quantitative analysis is carried out difficult. For this reason, at the former, in order to improve an SN ratio, the difference of a certain criteria signal and purpose signal (signal from the body tissue aiming at measurement) is taken, or it pretreats taking and standardizing that ratio etc., and the quantum of the component of the purpose of the target body tissue is performed by applying the multivariate-analysis technique.

[0022] moreover, the light from a certain light source which contains two or more wavelength by the conventional spectral-analysis approach -- an interference filter or a diffraction grating -- serial -- a spectrum -- carrying out -- the light by which the spectrum was carried out -- one

by one -- a ratio -- a measurement object is irradiated and it is asking for the absorbance and transmittance in each wavelength range by detecting the intensity of light penetrated or reflected, respectively. however, this technique -- a body tissue -- when it applies to measurement of description, it is detected as a spectrum which all the information that belongs to the constituent of the complicated body tissue which light penetrates or reflects superimposed -- ***** -- getting it blocked -- it becomes the spectrum with which the signal which originates in addition to the body tissue of the request which considers measurement as an intention (purpose) (attribution) was also contained. Therefore, the noise component to the signal which belongs to the component of the body tissue of the target request will increase, and an SN ratio will fall.

[0023] however, this invention top Norio body tissue -- description -- in a measuring device Since 1d of reflected lights reflected by the body tissue and reflected light 1e reflected with the reflecting mirror 4 are made to interfere and it was made to lead to a detector 5 The reflected light reflected light 1e reflected with the reflecting mirror 4 among 1d of reflected lights reflected by the body tissue and whose phase correspond can be strengthened, and it can lead to a detector 5. The noise component to the signal which belongs to the component of a body tissue which reflects the reflected light reflected light 1e reflected with the reflecting mirror 4 and whose phase correspond can be reduced, and an SN ratio can be raised.

[0024] The distance between the body tissue which reflects the reflected light reflected light 1e reflected with the reflecting mirror 4 and whose phase correspond, and reflected light 1e and the point in which 1d interferes mutually It is the distance and the match between a reflecting mirror 4, and said reflected light 1e and the point in which 1d interferes mutually. Therefore, it is detectable whether the reflected light reflected from the body tissue of the location of living body 3 throat is strengthened by interference by finding the distance between the points in which a reflecting mirror 4, said reflected light 1e, and 1d of reflected lights interfere.

[0025] Moreover, since the above-mentioned reflecting mirror 4 was formed free [migration] to 1d of reflected lights reflected by the body tissue, the location of the point in which reflected light 1e and 1d of reflected lights interfere, and a reflecting mirror 4 can be set up freely. Therefore, by moving a reflecting mirror 4 to the point in which above-mentioned reflected light 1e and 1d of reflected lights interfere The phase of the reflected light from the body tissue which exists in the location of the arbitration in a living body's 3 depth direction, and the phase of reflected light 1e reflected with a reflecting mirror 4 can be made in agreement. The reflected light from the body tissue of the request set as the object of measurement can be strengthened alternatively, the noise component to the signal which belongs to the component of a desired body tissue set as the object of measurement can be reduced, and an SN ratio can be raised.

[0026] the body tissue of this invention -- description -- a measuring device sets the quantum of the concentration of the body fluid component in a body tissue cell or besides a body tissue cell as one purpose. on the other hand, it is in the quantum of the concentration of this body fluid component among the near-infrared light 1 of the field (1250-1800nm) near the first overtone of water, and the near-infrared light 1 of the field (800-1300nm) near the second harmonic overtone of water -- it is -- it carries out by using both. As a property of each field, in the field near the first overtone of water, while the spectrum signal which belongs to molecular vibration is large, the permeability of light is bad, and while the spectrum signal which belongs to molecular vibration in the field near the second harmonic overtone of water is small, it is rich in the permeability of light.

[0027] moreover, when the quantum of the concentration of the above-mentioned body fluid component is a quantum of glucose concentration The coherent near-infrared light of at least one kind of wavelength which consists of a part of all fields chosen from the wavelength field (950-1150nm and 1250-1800nm), or fields as a near-infrared light 1 irradiated from the light source 9, Especially, it is necessary to use wavelength (945**20nm, 965**20nm, 1015**30nm, 1100**30nm, 1400**20nm, 1450**20nm, 1500**20nm, and 1680**20nm) of coherent near-infrared light.

[0028] In the quantum of glucose concentration, as a signal of the field near the first overtone of water, that is, 950-1150nm, Preferably 945**20nm, 965**20nm, 1015**30nm, It is necessary to measure preferably 1250-1800nm 1100**30nm, using at least one wave of a signal (1400**20nm, 1450**20nm, 1500**20nm, and 1680**20nm) as a signal of the field near the second harmonic overtone of water.

[0029] Thus, precision can carry out preferably 950–1150nm of 1250–1800nm of glucose concentration quantitative analysis to the quantum of glucose concentration by using at least one wave of a signal (1400**20nm, 1450**20nm, 1500**20nm, and 1680**20nm) (near-infrared light 1) for 945**20nm, 965**20nm, 1015**30nm, and 1100**30nm preferably, and measuring.

[0030] The signal of each measured wavelength is changed into glucose concentration with the information processing means 7 using the calibration curve (measuring type) created beforehand, and is displayed as measured value with a display 8. Although creation of a calibration curve (measuring type) is usually created using some kinds of wavelength, if said wavelength is included in this invention, neither measurement wavelength nor a number will be restricted.

[0031] Moreover, in order to carry out the quantum of the glucose concentration in a body tissue cell or besides a body tissue cell as a substitution property of the blood sugar level The location of a reflecting mirror 4 can be set up so that it may be made to interfere in 1d (scattered light) of reflected lights from the body tissue made the purpose which is in the location between 0.5–10.0mm preferably between 0.1–10.0mm hypodermically (object of measurement), and it is this. Precision can carry out glucose concentration as a substitution property of the blood sugar level quantitative analysis.

[0032] moreover, in performing a quantum for the quantum of concentration, especially glucose concentration of the body fluid component in a body tissue cell or besides a body tissue cell, reflected light 1e from a reflecting mirror 4 is made to interfere in 1d of reflected lights from the artery which flows near a living body's 3 body surface, or a vein, and it measures — it is a very good approach. If the location of a reflecting mirror 4 is adjusted and set up in that case so that the reflected light in the body tissue of the side near [where optical 1b of another side divided by the beam splitter 2 of the near-infrared light 1 is irradiated] the near blood vessel (i.e., the body surface close attendants of a blood vessel) may interfere with reflected light 1e from a reflecting mirror 4, since the flowing blood has the property that dispersion is large and cannot use a blood vessel for measurement easily, a good spectrum (signal) will be obtained.

[0033]

* NOTICES *

JPO and NCIP are not responsible for any damages caused by the use of this translation.

- 1.This document has been translated by computer. So the translation may not reflect the original precisely.
- 2.**** shows the word which can not be translated.
- 3.In the drawings, any words are not translated.

DESCRIPTION OF DRAWINGS

[Brief Description of the Drawings]

[Drawing 1] It is the schematic diagram showing the gestalt of 1 operation of this invention.

[Drawing 2] It is the schematic diagram showing the gestalt of other operations same as the above.

[Description of Notations]

1 Near-infrared Light

1a Light

1b Light

1c The reflected light in which it interfered

1d Reflected light

1e Reflected light

2 Beam Splitter

3 Living Body

4 Reflecting Mirror

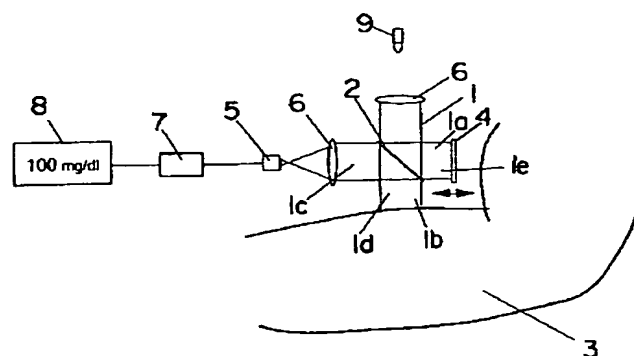
5 Detector

7 Information Processing Means

[Translation done.]

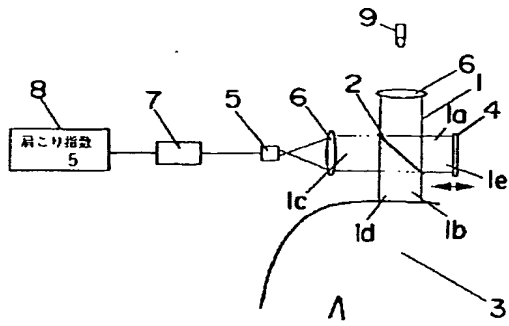
Drawing selection drawing 1

- 1 近赤外光
 1 a 光
 1 b 光
 1 c 干渉された反射光
 1 d 反射光
 1 e 反射光
 2 ビームスプリッター
 3 生体
 4 反射鏡
 5 検出器
 7 情報処理手段



[Translation done.]

Drawing selection drawing 2



[Translation done.]

(19)日本国特許庁 (J P)

(12) 公 開 特 許 公 報 (A)

(11)特許出願公開番号

特開平10-190

(43)公開日 平成10年(1998)1月6日

(51)Int.Cl. ⁹	識別記号	庁内整理番号	F I	技術表示箇所
A 6 1 B 5/14	3 1 0	0277-2 J	A 6 1 B 5/14	3 1 0
G 0 1 N 21/35			G 0 1 N 21/35	Z
33/483			33/483	

審査請求 未請求 請求項の数 8 O L (全 10 頁)

(21)出願番号 特願平8-154398

(22)出願日 平成 8 年(1996) 6 月14日

(71)出願人 000005832

松下電工株式会社

大阪府門真市大字門真1048番地

(72)発明者 丸尾 勝彦

大阪府門真市大字門真1048番地松下電工株式会社内

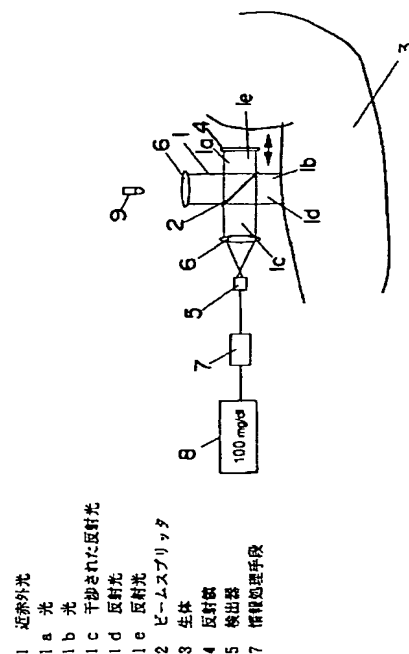
(74)代理人 弁理士 石田 長七 (外 2 名)

(54)【発明の名称】 生体組織性状測定装置

(57)【要約】

【課題】 成分や組織の濃度変化や物性変化に関連する信号をより明確にして正確な生体組織性状の定量分析あるいは定性分析をおこなうことができる生体組織性状測定装置を提供する。

【解決手段】 生体3中の生体組織性状を非侵襲的に計測する生体組織性状測定装置に関する。コヒーレントあるいはそれに近い近赤外光1を二つに分割するビームスプリッタ2。分割された近赤外光のうち一方の光1 aを生体組織で反射される他方の光1 bと干渉させるように反射する反射鏡4。干渉させた反射光1 cの信号を検出する検出器5。検出器5で検出された信号を演算処理する情報処理手段7とを備える。生体組織で反射された反射光1 dに対する反射鏡4の位置を設定自在に形成する。



【特許請求の範囲】

【請求項1】 生体中の生体組織性状を非侵襲的に計測する生体組織性状測定装置であって、コヒーレントあるいはそれに近い近赤外光を二つに分割するビームスプリッタと、分割された近赤外光のうち一方の光を生体組織で反射される他方の光と干渉させるように反射する反射鏡と、干渉させた反射光の信号を検出する検出器と、検出器で検出された信号を演算処理する情報処理手段とを備え、生体組織で反射された反射光に対する反射鏡の位置を設定自在に形成して成ることを特徴とする生体組織性状測定装置。

【請求項2】 前記生体組織性状が生体組織の細胞中あるいは生体組織の細胞外の体液成分濃度であることを特徴とする請求項1に記載の生体組織性状測定装置。

【請求項3】 前記生体組織性状である体液成分濃度がグルコース濃度であって、前記グルコース濃度の定量にあたって少なくとも950～1150nm及び1250～1800nmの領域から選択された全領域あるいは領域の一部からなる少なくとも一種類の波長のコヒーレント近赤外光を用いることを特徴とする請求項1又は2に記載の生体組織性状測定装置。

【請求項4】 皮下0.1～10.0mmの間の生体組織で反射された反射光に反射鏡で反射された反射光を干渉させるように前記反射鏡の位置を設定して成ることを特徴とする請求項1乃至3のいずれかに記載の生体組織性状測定装置。

【請求項5】 前記生体組織が体表面近傍の動脈血管あるいは静脈血管の体表側近傍であって、この生体組織で反射された反射光に反射鏡で反射された反射光を干渉させるように前記反射鏡の位置を設定して成ることを特徴とする請求項1乃至4のいずれかに記載の生体組織性状測定装置。

【請求項6】 所望の生体組織の組織性状を測定するのに好ましくない組織成分の光の吸収の大小の測定に基づいて、前記反射鏡の位置を設定して成ることを特徴とする請求項1乃至5のいずれかに記載の生体組織性状測定装置。

【請求項7】 前記好ましくない組織成分が脂肪組織であって、900～950nm及び1350～1420nmの少なくとも一方の波長領域の全領域あるいは領域の一部からなるコヒーレント近赤外光を用いると共に反射鏡を移動させることによって脂肪組織での上記コヒーレント近赤外光の吸収の大小を検出することを特徴とする請求項6に記載の生体組織性状測定装置。

【請求項8】 前記生体組織性状が生体組織の固さや密度等の物性であることを特徴とする請求項1に記載の生体組織性状測定装置。

【発明の詳細な説明】

【0001】

【発明の属する技術分野】 本発明は、健康管理や疾病の

治療のために、血液や細胞液などの体液中の指標成分の濃度を非侵襲で測定する計測機器に関するものであり、特に近赤外法を用いて血液中のグルコース、コレステロール、中性脂肪、蛋白成分などの濃度を非侵襲的に測定する生体組織性状測定装置、あるいは肩こりや乳癌、肝硬変、脂肪肝、動脈硬化に代表される生体組織の変化を測定する生体組織性状測定装置に関するものである。

【0002】

【従来の技術】 従来の体液成分濃度の測定に関して、血液中のグルコース濃度（血糖値）の測定方法を説明する。現在広く用いられている血糖計は、採血した血液中のグルコースを化学反応させてグルコース濃度を測定する、いわゆるバイオセンサと呼ばれるものである。基本的なバイオセンサは、測定対象成分を選択的に識別する部位と、この測定対象成分を選択的に識別する部位による物質識別で生じる変化を電気信号に変換する部位から構成されている。前記電気信号に変換する部位には、電気化学計測デバイス、サーミスタ、電界効果形トランジスタ(FET)、ホトトランジスタなどの多様なデバイスが用いられている。

【0003】 また物質識別部位（前記測定対象成分を選択的に識別する部位）に用いられる生体物質は、酵素(enzyme)、抗体(antibody)、結合タンパク質(binding protein)、レクチン(lectin)、細胞内小器官(organelle)、微生物などの細胞(cell)、組織(tissue)などで、これらの生体物質は特定の物質を識別する機能を有している。バイオセンサは利用する生体物質によって、酵素センサ、微生物センサ、免疫センサ、オルガネラ・センサ、組織センサに分類される。

【0004】 血糖計の例として酵素電極（生体物質として酵素を用いた物質識別部位）によるグルコースセンサを例に採ると、グルコース検知に使われる酵素は、グルコースオキシダーゼ(GOD)である。この酵素(GOD)を高分子膜などに固定化したグルコースセンサは、測定液中のグルコースがGOD固定化膜に接触することによって酸素が消費され、この酸素の変化をとらえることでグルコース濃度を定量する形式のものが開発されている。このような採血式の血糖計は広く市販され、糖尿病患者の血糖値の管理に利用されている。

【0005】 また採血を必要としない非侵襲のものとしては、特開昭60-236631号公報あるいは特公平5-58735号公報に示されているようなグルコースの検出方法がある。これらの公報には、生体部位に照射された近赤外光を基準信号と測定信号とに分け、これらの値を演算処理することにより血糖値を測定する手法が開示されている。上記手法において近赤外光の光源としては、タングステン・ハロゲンランプのような白色光源を干渉フィルタのような分光手段で所定の波長に分光する方法や半導体発光素子(LED)が用いられている。また生体部位を透過した近赤外光の検出器としては、フ

フォトダイオードあるいはフォトトランジスタのような受光素子が用いられている。しかしながら、現時点ではこれらの技術が実用レベルに達していない。

【0006】上記のような近赤外光による体液成分の分光分析は近年注目されている手法であり、中赤外領域における分光分析と比較して近赤外領域における分光分析では、水の吸収スペクトルが小さいので、水溶液系の分析が可能であることや、生体を透過する能力が高いという長所を有する反面、分子振動に帰属する信号レベルが中赤外領域と比較して100分の1程度と小さいことや、信号の帰属が特定しにくいという短所を有するものである。

【0007】すなわち、近赤外領域において目的とする成分（体液成分）のシグナル（信号）を検知する場合、目的とする成分（体液成分）の濃度変化に対応する信号が非常に小さいこと、またその信号の帰属が明瞭でない場合が多いという問題を抱えている。このような問題を解決するために統計解析手法あるいは多変量解析手法、例えば線形重回帰分析（MLR）、主成分重回帰分析、PLS重回帰分析（partial least squares regression）と組み合わせるいわゆるケモメトリクス手法が用いられている。しかしこれらの統計的解析手法は微小な信号変化をとらえ、正確な検量（キャリブレーション）をおこなうのに優れた手法ではあるが、目的の成分（体液成分）のシグナル（信号）の大きさ（SN比）を改善するものではない。

【0008】そこで従来では近赤外領域におけるSN比の改善のために、基準信号と目的の成分（体液成分）の濃度変化に係る信号との差、あるいはそれらの比をとることにより目的の成分（体液成分）の濃度変化（変動）を明確にしたり、複数回計測した信号（目的の成分（体液成分）の濃度変化に係る信号）を平均化することによりノイズ成分を小さくしたりする手法が用いられている。特に上記平均化手法は、平均回数（信号の計測回数）を多くすることで簡単にノイズ成分の除去が可能であることから様々な測定に利用されている。

【0009】また生体組織に単に光を入射させてその透過光あるいは反射光を測定する従来の方法では、性状の定量化を意図とする目的の生体組織以外の組織からの透過光あるいは反射光が重畳した形で信号として測定されることになってしまい、ノイズ成分が大きくなる原因となっている。そこで性状測定において、性状の定量化を意図とする目的の生体組織からの透過光あるいは反射光のみが得られるように、目的とする組織をねらい打つ形のスペクトル測定（分光分析測定）をおこなうことができるような手法の確立や装置が望まれている。

【0010】

【発明が解決しようとする課題】従って本発明は、生体の体液成分の濃度を測定する際に、血液あるいは細胞液などを注射針などで侵襲して取り出す必要のない非侵襲

の生体組織性状測定装置、あるいは生体内組織の固さや密度等の物性を非侵襲、非接触的に計測する生体組織性状測定装置を提供することを目的とするものであり、詳しくは、近赤外分光分析法を生体組織性状測定に適用して組織中の目的の成分の定量あるいは定性分析をおこなう場合において、分析を目的とする組織あるいは組織近傍からの反射光を選択的に検知することで、成分や組織の濃度変化や物性変化に関連する信号をより明確にして正確な生体組織性状の定量分析あるいは定性分析をおこなうことができる生体組織性状測定装置を提供することを目的とするものである。

【0011】

【課題を解決するための手段】本発明の請求項1に記載の生体組織性状測定装置は、生体3中の生体組織性状を非侵襲的に計測する生体組織性状測定装置であって、コヒーレントあるいはそれに近い近赤外光1を二つに分割するビームスプリッター2と、分割された近赤外光のうち一方の光1aを生体組織で反射される他方の光1bと干渉させるように反射する反射鏡4と、干渉させた反射光1cの信号を検出する検出器5と、検出器5で検出された信号を演算処理する情報処理手段7とを備え、生体組織で反射された反射光1dに対する反射鏡4の位置を設定自在に形成して成ることを特徴とするものである。

【0012】また本発明の請求項2に記載の生体組織性状測定装置は、請求項1の構成に加えて、前記生体組織性状が生体組織の細胞中あるいは生体組織の細胞外の体液成分濃度であることを特徴とするものである。また本発明の請求項3に記載の生体組織性状測定装置は、請求項1又は2の構成に加えて、前記生体組織性状である体液成分濃度がグルコース濃度であって、前記グルコース濃度の定量にあたって少なくとも950～1150nm及び1250～1800nmの領域から選択された全領域あるいは領域の一部からなる少なくとも一種の波長のコヒーレント近赤外光を用いることを特徴とするものである。

【0013】また本発明の請求項4に記載の生体組織性状測定装置は、請求項1乃至3のいずれかの構成に加えて、皮下0.1～10.0mmの間の生体組織で反射された反射光1dに反射鏡4で反射された反射光1eを干渉させるように前記反射鏡4の位置を設定して成ることを特徴とするものである。また本発明の請求項5に記載の生体組織性状測定装置は、請求項1乃至4のいずれかの構成に加えて、前記生体組織が体表面近傍の動脈血管あるいは静脈血管の体表側近傍であって、この生体組織で反射された反射光1dに前記反射鏡4で反射された反射光1eを干渉させるように前記反射鏡4の位置を設定して成ることを特徴とするものである。

【0014】また本発明の請求項6に記載の生体組織性状測定装置は、請求項1乃至5のいずれかの構成に加えて、所望の生体組織の組織性状を測定するのに好ましく

ない組織成分の光の吸収の大小の測定に基づいて、反射鏡4の位置を設定して成ることを特徴とするものである。また本発明の請求項7に記載の生体組織性状測定装置は、請求項6に記載の構成に加えて、前記好ましくない組織成分が脂肪組織であって、900～950nm及び1350～1420nmの少なくとも一方の波長領域の全領域あるいは領域の一部からなるコヒーレント近赤外光1を用いると共に反射鏡4を移動させることによって脂肪組織での前記コヒーレント近赤外光1の吸収の大小を検出することを特徴とするものである。

【0015】また本発明の請求項8に記載の生体組織性状測定装置は、請求項1の構成に加えて、前記生体組織性状が生体組織の固さや密度等の物性であることを特徴とするものである。

【0016】

【発明の実施の形態】以下、本発明の実施の形態を説明する。図1に示す生体組織性状測定装置において使用する光源9としては、750～2500nmの波長でコヒーレントあるいはそれに近い近赤外光1を得られるものであれば何れでも用いることができ、例えばレーザー光源、ハロゲンランプの光を回折格子や干渉計やフィルター等を利用して処理したもの、LED光源あるいはLED光源の光を回折格子や干渉計やフィルター等を利用して処理したものなどを用いることができる。

【0017】ビームスプリット2としては、ハーフミラー等の上記近赤外光1を二つに分割することができるものであれば何れでも用いることができ、このビームスプリット2は上記光源9と生体3の間に配置されている。反射鏡4としては、上記ビームスプリット2で二つに分割された光のうちの一方の光1aを反射するものであって、この一方の光1aが導かれて到達する位置に配置されている。また反射鏡4は後述する生体3中の生体組織で反射された反射光1dに対する位置を変更して自由に設定することができるように移動自在に形成されている。

【0018】検出器5としては、近赤外領域（近赤外光1）に受光特性を有するものであればよいが、波長が600～1100nmの近赤外領域ではSi製のディテクターが、波長が700～1700nmの近赤外領域ではInGaAs製のディテクターが特に好適に用いることができる。演算処理手段7としては、検出器5で得られる後述する干渉された反射光1cからの信号が入力されてこの信号を演算処理することができるものであれば何れでも使用することができ、マイクロコンピュータなどを例示することができる。

【0019】上記演算処理手段7では、検出器5で得られる干渉された反射光1cからの信号を予め用意された検量線にしたがって演算処理して生体性状、例えばグルコース濃度などを算出するものである。検量線（検量式）の作成には、統計的解析手法あるいは多変量解析手

法、例えば線形重回帰分析（MLR）、主成分回帰分析、PLS回帰分析（partial least squares regression）、ニューラルネット手法を用いることができる。これらの統計的解析手法は微小な信号変化をとらえ、正確な検量（キャリブレーション）をおこなうのに優れた手法である。

【0020】次に上記生体組織性状測定装置の動作について説明する。まず光源9から照射された近赤外光1はビームスプリット2によって、反射鏡4の方向に導かれる光1aと、生体3の方向に導かれる光1bとに分割される。次に反射板4の方向に導かれた光1aは反射鏡4で反射されて反射光1eとなると共に生体3の方向に導かれた光1bは生体3の内部の生体組織で反射されて散乱光である反射光1dとなる。次に生体組織で反射された反射光1dと反射鏡4で反射された反射光1eとが干渉し、この干渉した反射光1cが検出器5に導かれる。そして次に検出器5に導かれた干渉された反射光1cから得られる信号を情報処理手段7で上記のように演算処理することによって、測定を目的とする所望の生体組織の性状を定量して測定することができるのである。

【0021】上述のように従来からおこなわれている750～2500nmの波長の近赤外光（近赤外領域）を用いた分光分析方法は、一般的に目的とする成分に関連するシグナル（信号）が小さく、その帰属が明確でない場合が多いので定量分析が困難であるとされている。このために従来ではSN比を改善するために、ある基準シグナルと目的シグナル（測定を目的とする生体組織からのシグナル）との差をとったり、その比をとって規格化するなどの前処理をし、多変量解析手法を応用することで目的の生体組織の目的の成分の定量をおこなっている。

【0022】また従来の分光分析方法では、複数の波長を含むある光源からの光を干渉フィルターあるいは回折格子により時系列的に分光し、その分光された光を順次、比測定物に照射し、透過あるいは反射した光の強さを検知することによって、各波長帯における吸光度や透過度をそれぞれ求めている。しかしこの手法を生体組織性状の測定に適用した場合、光が透過あるいは反射する複雑な生体組織の構成成分に帰属するすべての情報が重畳したスペクトルとして検出されることになり、つまりは測定を意図（目的）とする所望の生体組織以外に由来（帰属）するシグナルも含まれたスペクトルとなる。そのために目的とする所望の生体組織の成分に帰属するシグナルに対するノイズ成分が増大してSN比が低下してしまうのである。

【0023】しかし本発明の上記生体組織性状測定装置では、生体組織で反射された反射光1dと反射鏡4で反射された反射光1eとを干渉させて検出器5に導くようにしたので、生体組織で反射された反射光1dのうち反射鏡4で反射された反射光1eと位相が一致する反射光

を強めて検出器5に導くことができ、反射鏡4で反射された反射光1eと位相が一致する反射光を反射する生体組織の成分に帰属するシグナルに対するノイズ成分を低減させてSN比を向上させることができるのである。

【0024】反射鏡4で反射された反射光1eと位相が一致する反射光を反射する生体組織と反射光1e、1dが互いに干渉する点との間の距離は、反射鏡4と前記反射光1e、1dが互いに干渉する点との間の距離と一致するものであり、従って反射鏡4と前記反射光1e及び反射光1dが干渉する点との間の距離を求めることによって生体3のどの位置の生体組織から反射された反射光が干渉によって強められているかを検知することができる。

【0025】また上記反射鏡4は生体組織で反射された反射光1dに対して移動自在に形成したので、反射光1e及び反射光1dが干渉する点と反射鏡4の位置を自由に設定することができるものである。従って反射鏡4を上記反射光1e及び反射光1dが干渉する点に対して移動させることによって、生体3の深さ方向における任意の位置に存在する生体組織からの反射光の位相と反射鏡4で反射される反射光1eの位相とを一致させることができ、測定の対象となる所望の生体組織からの反射光を選択的に強めることができるものであり、このために測定の対象となる所望の生体組織の成分に帰属するシグナルに対するノイズ成分を低減させてSN比を向上させることができるのである。

【0026】本発明の生体組織性状測定装置は、生体組織細胞中あるいは生体組織細胞外の体液成分の濃度の定量を一つの目的とするものである。この体液成分の濃度の定量には、水の第一倍音付近の領域(1250~1800nm)の近赤外光1と、水の第二倍音付近の領域(800~1300nm)の近赤外光1のうち、一方あるいは両方を利用することによっておこなう。各領域の特性としては、水の第一倍音付近の領域では、分子振動に帰属するスペクトル信号が大きい反面、光の透過性が悪く、水の第二倍音付近の領域では、分子振動に帰属するスペクトル信号が小さい反面、光の透過性に富むのである。

【0027】また上記体液成分の濃度の定量がグルコース濃度の定量である場合には、光源9から照射される近赤外光1としては、950~1150nm及び1250~1800nmの波長領域から選択した全領域あるいは領域の一部からなる少なくとも一種の波長のコヒーレント近赤外光、特に、945±20nm、965±20nm、1015±30nm、1100±30nm、1400±20nm、1450±20nm、1500±20nm、1680±20nmの波長のコヒーレント近赤外光を用いる必要がある。

【0028】つまりグルコース濃度の定量には、水の第一倍音付近の領域の信号として950~1150nm、

好ましくは945±20nm、965±20nm、1015±30nm、1100±30nmを、水の第二倍音付近の領域の信号として1250~1800nm、好ましくは1400±20nm、1450±20nm、1500±20nm、1680±20nmのシグナルの少なくとも一波長を用いて測定する必要がある。

【0029】このようにグルコース濃度の定量に950~1150nm、好ましくは945±20nm、965±20nm、1015±30nm、1100±30nmを、1250~1800nm、好ましくは1400±20nm、1450±20nm、1500±20nm、1680±20nmのシグナル(近赤外光1)の少なくとも一波長を用いて測定することによって、グルコース濃度を精度よく定量分析することができるものである。

【0030】測定された各波長の信号は、前もって作成された検量線(検量式)を用いて情報処理手段7でグルコース濃度に変換されて、表示装置8で測定値として表示される。検量線(検量式)の作成は通常数種類の波長を用いて作成されるが、本発明においては前記波長を含むものであれば、測定波長や数のいずれも制限するものではない。

【0031】また血糖値の代用特性として生体組織細胞中あるいは生体組織細胞外のグルコース濃度を定量するには、皮下0.1~10.0mmの間、好ましくは0.5~10.0mmの間の位置にある目的とする(測定の対象の)生体組織からの反射光(散乱光)1dに干渉させるように反射鏡4の位置を設定することができ、このことで、血糖値の代用特性としてのグルコース濃度を精度よく定量分析することができるものである。

【0032】また生体組織細胞中あるいは生体組織細胞外の体液成分の濃度の定量、特にグルコース濃度を定量をおこなうにあたっては、生体3の体表面近傍を流れる動脈あるいは静脈からの反射光1dに反射鏡4からの反射光1eを干渉させて測定するの非常に良い方法である。その際血管を流れる血液は散乱が大きい特性があつて測定に利用しにくいので、近赤外光1のビームスプリッタ2で分割された他方の光1bが照射される側の血管近傍、つまり血管の体表面側近傍の生体組織での反射光が反射鏡4からの反射光1eと干渉するように反射鏡4の位置を調整して設定すると、良いスペクトル(信号)が得られる。

【0033】またSN比の良い(高い)スペクトルを得るという観点から、グルコース濃度の定量には皮下脂肪組織を避けて測定をおこなう必要がある。そのために、反射鏡4の位置を移動させて測定における適切な設定位置を見つけることは非常に有効であり、その脂肪組織の位置を検出するにあたっては、グルコース濃度の定量に好ましくない脂肪組織の特徴的な光の吸収を用いておこなう。この脂肪組織での光の吸収の大小の測定をおこなうにあたっては、少なくとも900~950nmあるい

は1350～1420nmの波長領域の全領域あるいは領域の一部からなるコヒーレント近赤外光1を用いておこない、この吸収が脂肪組織によるものか否かを比較して判断する。

【0034】本発明の生体組織性状測定装置のもう一つの目的は、生体組織性状が生体組織の固さや密度のような物性であって、この物性を定性分析あるいは定量分析することにある。生体組織の固さや密度のような物性とは、具体的には肩こりに代表される身体のこり、あるいは乳癌や肝硬変や脂肪肝や動脈硬化に代表される生体組織の変化である。

【0035】このような生体組織性状の分析には、多数の被験者から得られるスペクトルを定量分析あるいは定性分析を利用しておこなわれる。定量分析には線形重回帰分析(MLR)、主成分回帰分析、PLS回帰分析(partial least squares regression)、ニューラルネットワーク手法、ニューラルネットワーク手法が用いられ、定性分析には判別分析、クラスタ分析等の手法が利用することができる。

【0036】生体組織の固さや密度のような物性を分析(測定)する生体組織性状測定装置も上記と同様に形成することができる。分析に利用する光源9から照射される近赤外光1の波長や情報処理手段7における検量手法の決定は、多数の正常組織と病変組織のスペクトル(信号)を解析することによりおこなうが、分析に利用する光源9から照射される近赤外光1の波長や情報処理手段7における検量手法の他の決定手法としては、予め動物実験等により侵襲的におこなう方法がある。この方法は侵襲的に露出させた被測定組織(正常組織及び病変組織の両方)に回折格子やFT-IR等の手法により分光した光を照射して吸収スペクトルを得て、この吸収スペクトルを多変量解析することにより、本発明の生体組織性状測定装置に利用する近赤外光1の波長や情報処理手段7における検量手法を決定し、この決定した近赤外光1の波長や情報処理手段7における検量手法を利用して上述のように本発明の生体組織性状測定装置による生体組織性状の測定(in vivo 測定)をおこなうようにする。

【0037】具体例を挙げると、人為的に癌化させたマウスの癌組織を表皮組織を切開することにより露出させ、上記手法で癌組織のスペクトルを得る。また同様の操作を正常なマウスを含む多数のマウスに実施してスペクトルを得、次にこれらスペクトルを定性分析することにより、組織性状の判別に意味のある波長をピックアップして、本発明の生体組織性状測定装置に利用する近赤外光1の波長を決定する。そしてこの決定した波長の近赤外光1を本発明の生体組織性状測定装置による生体組織の性状の分析をおこなうことによって、生体組織で癌発症を判別することができる。

【0038】尚、本発明の生体組織性状測定装置の分析精度を上げるには、さらに本発明の生体組織性状測定装

置による分析を非侵襲的に多数の生体組織に施して、多変量解析する必要がある。また上にも述べたが、本発明の生体組織性状測定装置を用いて侵襲的な実験を経ずに非侵襲的な段階から分析を実施しても、生体組織の固さや密度のような物性を分析することは可能である。

【0039】次に本発明の生体組織性状測定装置の実施例を説明する。図1に示す生体組織性状測定装置は、生体組織性状として生体組織中のグルコース濃度を測定するものである。光源9として1670nmと1450nmの波長のコヒーレント近赤外光1を照射するコヒーレントレーザ光源を用いている。6は光源9から照射されたコヒーレント近赤外光1を集光する凸型のレンズである。光源9から照射されたコヒーレント近赤外光1を二つに分割するビームスプリッタ2は、レンズ6と被測定物である生体(腕)3の間に配置されており、レンズ6を介して照射されるコヒーレント近赤外光1の進行方向に対して約45°傾けられている。レンズ6を介してビームスプリッタ2に照射されたコヒーレント近赤外光1は、このコヒーレント近赤外光1の進行方向に対して約90°に進行する光1aと、コヒーレント近赤外光1の進行方向と略平行な方向に進行する光1bとに分割され、上記光1aはコヒーレント近赤外光1の進行方向と略平行に配置される反射鏡4に導かれると共に上記光1bは生体3に導かれる。図1に矢印で示すように反射鏡4は上記スプリッタ2に対して近接離隔するように移動自在に形成されている。

【0040】上記光1aは反射鏡4でビームスプリッタ2の方に反射光1eとして反射されると共に上記光1bは生体3中の任意の位置の生体組織でビームスプリッタ2の方に反射光1dとして反射され、両方の反射光1e、1dはビームスプリッタ2の位置で互いに干渉するが、皮下2mmに位置する生体組織からの反射光の位相と反射鏡4からの反射光1eの位相とが一致するように(干渉するように)、ビームスプリッタ2(反射光1d、1eの干渉の位置)からの反射鏡4の位置を設定してある。このように皮下2mmに位置する生体組織からの反射光の位相と反射鏡4からの反射光1eの位相とが一致するようにビームスプリッタ2の干渉の位置からの反射鏡4の位置を設定することによって、皮下2mmに位置する生体組織からの反射光を選択的に強めることができる。

【0041】この干渉した反射光1cは反射板4と略正面向向する凸型のレンズ10で集光されて検出器(受光素子)5に導かれる。この後検出器5で電圧に変換された反射光1cからの信号をデジタル化してマイクロコンピュータである情報処理手段7に入力し、上記信号を予め用意された検量線に従って情報処理手段7で演算処理することによってグルコース濃度が算出され、このグルコース濃度が測定値として表示手段8に表示されるようになっていく。

【0042】グルコース濃度を算出するために使用する検量線は、本発明の利用者あるいは複数の人間を被験者とし、本発明とは異なる他の標準手法により得られるグルコース濃度の真値と、本発明によるコヒーレント近赤外光1の吸光度の関係を統計的解析手段により解析することで得ることができる。また上記他の標準手法での生体組織のグルコース濃度の定量が困難な場合は、代用特性として血液中のグルコース濃度(血糖値)を用いて検量線を作成してもよい。この場合、本発明を逆に血糖値測定装置として利用することができる。

【0043】また本発明の利用者本人より検量線を作成する場合にあたっては、グルコース負荷試験を用いることができる。これは先ずグルコース含有物を飲料後、一定時間間隔で採血と上記本発明による信号測定をおこなうようにする。次に採血した血液を分析する標準手法により得られたグルコース濃度と、本発明の測定時に記憶された信号とを対比してデータ化し、このデータを用いて情報処理手段7に内蔵される解析手段により検量線が作成される。この実施例において個人対応の検量線を作成する場合には重回帰分析手法を用いている。

【0044】次に他の実施例を説明する。この実施例のものは生体組織性状として生体組織中のグルコース濃度を測定するものである。光源9としてはタングステンハロゲンランプと回折格子からなる光源を用いており、この回折格子を用いることによって950～1150nmの波長領域のスペクトルを測定してグルコースの定量をおこなうようにしている。また皮下2mmに位置する生体組織からの反射光の位相と反射鏡4からの反射光1eの位相とが一致するように(干渉するように)反射鏡4の位置が設定されている。これら以外は上記実施例と同様に図1に示すように形成されている。

【0045】またグルコース濃度を算出するために使用する検量線は、本発明の利用者あるいは複数の人間を被験者とし、本発明とは異なる他の標準手法により得られるグルコース濃度の真値と、本発明によるコヒーレント近赤外光1の吸光度の関係を統計的解析手段により解析することで得た。またこの実施例において個人対応の検量線を作成する場合にはPLS回帰分析手法を用いている。

【0046】次にさらに他の実施例を説明する。この実施例のものは生体組織性状として生体組織中のグルコース濃度を測定するものである。光源9としてはタングステンハロゲンランプと回折格子からなる光源を用いており、この回折格子を用いることによって1250～1800nmの波長領域のスペクトルを測定してグルコースの定量をおこなうようにしている。また皮下2mmに位置する生体組織からの反射光の位相と反射鏡4からの反射光1eの位相とが一致するように(干渉するように)反射鏡4の位置が設定されている。これら以外は上記実施例と同様に図1に示すように形成されている。

【0047】またグルコース濃度を算出するために使用する検量線は、本発明の利用者あるいは複数の人間を被験者とし、本発明とは異なる他の標準手法により得られるグルコース濃度の真値と、本発明によるコヒーレント近赤外光1の吸光度の関係を統計的解析手段により解析することで得た。またこの実施例において個人対応の検量線を作成する場合にはPLS回帰分析手法を用いている。

【0048】次にさらに他の実施例を説明する。この実施例のものは生体組織性状として生体組織中のグルコース濃度を測定するものである。光源9としてはタングステンハロゲンランプと干渉フィルタからなる光源を用いており、使用した干渉フィルタは中心波長が1400nm、1500nm、1680nmで半値幅が20nmのものであった。また皮下2mmに位置する生体組織からの反射光の位相と反射鏡4からの反射光1eの位相とが一致するように(干渉するように)反射鏡4の位置が設定されている。これら以外は上記実施例と同様に図1に示すように形成されている。

【0049】またグルコース濃度を算出するために使用する検量線は、本発明の利用者あるいは複数の人間を被験者とし、本発明とは異なる他の標準手法により得られるグルコース濃度の真値と、本発明によるコヒーレント近赤外光1の吸光度の関係を統計的解析手段により解析することで得た。またこの実施例において個人対応の検量線を作成する場合には重回帰分析手法を用いている。

【0050】次にさらに他の実施例を説明する。この実施例のものは生体組織性状として生体組織中のグルコース濃度を測定するものである。光源9としてはタングステンハロゲンランプと干渉フィルタからなる光源を用いており、使用した干渉フィルタは中心波長が945nm、965nm、1015nm、1100nmで半値幅が20nmのものであった。また皮下2mmに位置する生体組織からの反射光の位相と反射鏡4からの反射光1eの位相とが一致するように(干渉するように)反射鏡4の位置が設定されている。これら以外は上記実施例と同様に図1に示すように形成されている。

【0051】またグルコース濃度を算出するために使用する検量線は、本発明の利用者あるいは複数の人間を被験者とし、本発明とは異なる他の標準手法により得られるグルコース濃度の真値と、本発明によるコヒーレント近赤外光1の吸光度の関係を統計的解析手段により解析することで得た。またこの実施例において個人対応の検量線を作成する場合には重回帰分析手法を用いている。

【0052】次にさらに他の実施例を説明する。この実施例のものは生体組織性状として生体組織中のグルコース濃度を測定するものである。光源9としてはタングステンハロゲンランプと回折格子からなる光源を用いており、この回折格子を用いることによって1250～1800nmの波長領域のスペクトルを測定することにより

グルコース濃度の定量をおこなっている。またこの実施例では、近赤外光1から分割された光1bを生体(腕)3の皮静脈に向けて照射し、静脈血の反射スペクトルを測定するようにしている。反射鏡4の位置は上記皮静脈血管の体表面側の面からの反射光の位相と反射鏡4からの反射光1eの位相とが一致するように(干渉するように)調節して設定されている。このような反射鏡4の位置は、血液の散乱が大きいことを利用して反射鏡4の位置を調節して、皮静脈血管の体表面側の面からの反射光において大きなゲイン(利得)が得られるところで固定するようにしている。これら以外は上記実施例と同様に図1に示すように形成されている。

【0053】またグルコース濃度を算出するために使用する検量線は、本発明の利用者あるいは複数の人間を被験者とし、本発明とは異なる他の標準手法により得られるグルコース濃度の真値と、本発明によるコヒーレント近赤外光1の吸光度の関係を統計的解析手段により解析することで得た。またこの実施例において個人対応の検量線を作成する場合にはPLS回帰分析手法を用いている。

【0054】次にさらに他の実施例を説明する。この実施例のものは生体組織性状として生体組織中のグルコース濃度を測定するものである。光源9としてはタングステンハロゲンランプと回折格子からなる光源を用いており、この回折格子を用いることによって950～1150nmの波長領域のスペクトルを測定することによりグルコース濃度の定量をおこなっている。またこの実施例ではグルコース濃度の測定に先立ち、900～950nmの近赤外光1を用いて上記と同様のスペクトルの測定をおこない、これにより脂肪組織での反射光1dであるか否かを判定し、脂肪組織でのスペクトルでないことを確認している。この判定には定性分析手法を利用した。これら以外は上記実施例と同様に図1に示すように形成されている。

【0055】またグルコース濃度を算出するために使用する検量線は、本発明の利用者あるいは複数の人間を被験者とし、本発明とは異なる他の標準手法により得られるグルコース濃度の真値と、本発明によるコヒーレント近赤外光1の吸光度の関係を統計的解析手段により解析することで得た。またこの実施例において個人対応の検量線を作成する場合にはPLS回帰分析手法を用いている。

【0056】次にさらに他の実施例を図2に基づいて説明する。この実施例のものは生体(肩)3の生体組織性状として肩こりを測定するものである。光源9としてはタングステンハロゲンランプと回折格子からなる光源を用いており、この回折格子を用いることによって950～1150nmの波長領域のスペクトルを測定することにより生体組織の固さの定性分析をおこなっている。またこの実施例ではビームプリット2で分割された光1b

を肩部分に照射し、これにて得られるスペクトルを上記と同様に分析して定性分析を実施している。これら以外は上記実施例と同様に図1に示すように形成されている。

【0057】また肩こりの程度を算出するために使用する検量線は、本発明の利用者あるいは複数の人間を被験者とし、本発明とは異なる他の標準手法により得られる肩こりの程度と、本発明によるコヒーレント近赤外光1の吸光度の関係を統計的解析手段により解析することで得た。肩こりの程度はプロのマッサージ師による触診から得られる5段階評価の値を用いた。またこの実施例において個人対応の検量線を作成する場合にはPLS回帰分析手法を用いている。

【0058】

【発明の効果】上記のように本発明の請求項1に記載の発明は、コヒーレントあるいはそれに近い近赤外光を二つに分割するビームスプリットと、分割された近赤外光のうち一方の光を生体組織で反射される他方の光と干渉させるように反射する反射鏡と、干渉させた反射光の信号を検出する検出器と、検出器で検出された信号を演算処理する情報処理手段とを備え、生体組織で反射された反射光に対する反射鏡の位置を設定自在に形成したので、分割された近赤外光のうち一方の光を生体組織で反射される他方の光と干渉させるように反射鏡で反射することによって、反射鏡で反射された反射光の位相と一致する位相の生体組織で反射された反射光を選択的に強めることができ、反射鏡で反射された反射光の位相と一致する位相の反射光を反射する生体組織の性状分析を非侵襲で精度良く分析することができる、つまり生体組織の成分や組織の濃度変化や物性変化に関連する信号をより明確にして正確な生体組織性状の定量分析あるいは定性分析をおこなうことができるものである。

【0059】しかも生体組織で反射された反射光に対する反射鏡の位置を設定自在に形成することによって、生体の任意の位置の生体組織からの反射光の位相と反射鏡で反射された反射光の位相とを一致させることができ、生体の任意の位置の分析を目的とする組織あるいは組織近傍からの反射光を選択的に検知することができるものである。

【0060】また本発明の請求項2に記載の発明は、前記生体組織性状が生体組織の細胞中あるいは生体組織の細胞外の体液成分濃度であるので、生体組織の細胞中あるいは生体組織の細胞外の体液成分濃度を非侵襲で精度良く分析することができるものである。また本発明の請求項3に記載の発明は、前記生体組織性状である体液成分濃度がグルコース濃度であって、前記グルコース濃度の定量にあたって少なくとも950～1150nm及び1250～1800nmの領域から選択された全領域あるいは領域の一部からなる少なくとも一種の波長のコヒーレント近赤外光を用いたので、グルコース濃度を非侵襲で精度良く分析することができるものである。

【0061】また本発明の請求項4に記載の発明は、皮下0.1～10.0mmの間の生体組織で反射された反射光に反射鏡で反射された反射光を干渉させるように前記反射鏡の位置を設定したので、血糖値の代用特性として生体組織のグルコース濃度を測定するにあたって、グルコース濃度を非侵襲で精度良く分析することができるものである。

【0062】また本発明の請求項5に記載の発明は、前記生体組織が体表面近傍の動脈血管あるいは静脈血管の体表側近傍であって、この生体組織で反射された反射光に反射鏡で反射された反射光を干渉させるように前記反射鏡の位置を設定したので、散乱の小さい体表面近傍の動脈血管あるいは静脈血管の体表側近傍からの反射光の位相と反射鏡で反射された反射光の位相を一致させることによって、散乱の大きい血液からの反射光の位相と反射鏡で反射された反射光の位相を一致させる場合よりも、生体性状、特にグルコース濃度を非侵襲で精度良く分析することができるものである。

【0063】また本発明の請求項6に記載の発明は、所望の生体組織の組織性状を測定するのに好ましくない組織成分の光の吸収の大小の測定に基づいて、前記反射鏡の位置を設定したので、所望の生体組織の組織性状を測定するのに好ましくない組織成分からの反射光の位相と反射鏡で反射された反射光の位相を一致させないようにすることができ、生体性状を非侵襲で精度良く分析することができるものである。

【0064】また本発明の請求項7に記載の発明は、前

記好ましくない組織成分が脂肪組織であって、900～950nm及び1350～1420nmの少なくとも一方の波長領域の全領域あるいは領域の一部からなるコヒーレント近赤外光を用いると共に反射鏡を移動させることによって脂肪組織での上記コヒーレント近赤外光の吸収の大小を検出したので、脂肪組織からの反射光であるか否かを精度良く分析することができるものである。

【0065】また本発明の請求項8に記載の発明は、前記生体組織性状が生体組織の固さや密度等の物性であるので、生体組織の性状のうち上記物性の分析を非侵襲で精度良く分析することができるものである。

【図面の簡単な説明】

【図1】本発明の一実施の形態を示す概略図である。

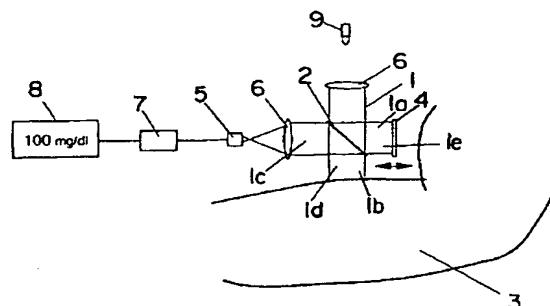
【図2】同上の他の実施の形態を示す概略図である。

【符号の説明】

- 1 近赤外光
- 1a 光
- 1b 光
- 1c 干渉された反射光
- 1d 反射光
- 1e 反射光
- 2 ビームスプリッタ
- 3 生体
- 4 反射鏡
- 5 検出器
- 7 情報処理手段

【図1】

- 1 近赤外光
- 1a 光
- 1b 光
- 1c 干渉された反射光
- 1d 反射光
- 1e 反射光
- 2 ビームスプリッタ
- 3 生体
- 4 反射鏡
- 5 検出器
- 7 情報処理手段



**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☒ FADED TEXT OR DRAWING
- ☒ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☒ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☒ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.